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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/997,424	11/28/2001	Kimberly A. Gillis	102729-16	6432
21125	7590	12/04/2003	EXAMINER	
NUTTER MCCLENNEN & FISH LLP WORLD TRADE CENTER WEST 155 SEAPORT BOULEVARD BOSTON, MA 02210-2604			DAVIS, MINH TAM B	
		ART UNIT	PAPER NUMBER	
		1642	JL	
DATE MAILED: 12/04/2003				

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	09/997,424	GILLIS ET AL.
	<b>Examiner</b>	<b>Art Unit</b>
	MINH-TAM DAVIS	1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### **Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

1)  Responsive to communication(s) filed on 02 September 2003.

2a)  This action is **FINAL**.                            2b)  This action is non-final.

3)  Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

4)  Claim(s) 1-33 is/are pending in the application.  
4a) Of the above claim(s) 8-10 and 16-33 is/are withdrawn from consideration.

5)  Claim(s) \_\_\_\_\_ is/are allowed.

6)  Claim(s) 1-7 and 11-15 is/are rejected.

7)  Claim(s) \_\_\_\_\_ is/are objected to.

8)  Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

9)  The specification is objected to by the Examiner.

10)  The drawing(s) filed on \_\_\_\_\_ is/are: a)  accepted or b)  objected to by the Examiner.

    Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

    Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)  The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

12)  Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a)  All b)  Some \* c)  None of:  
1.  Certified copies of the priority documents have been received.  
2.  Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3.  Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.

13)  Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a)  The translation of the foreign language provisional application has been received.

14)  Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

- 1)  Notice of References Cited (PTO-892)
- 2)  Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3)  Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3,9 .

4)  Interview Summary (PTO-413) Paper No(s). 12 (2 interviews)  
5)  Notice of Informal Patent Application (PTO-152)  
6)  Other: \_\_\_\_\_

### **DETAILED ACTION**

In a telephonic interview with Jasbir Sagoo on 11.21/03, Applicant asserts that in the response of paper No:11 on 09/02/03, Applicant does not intend to elect all of groups 25-48, but rather Applicant means to elect only one group, group 26, claims 1-7, 11-16, as drawn to a method of detecting prostate cancer, comprising determining the mRNA level of SMARCD3, with traverse.

Applicant's election with traverse of group 26, Claims 1-7, 11-16, SMARCD3 in Paper No.11 is acknowledged and entered. Affirmation of this election must be made by Applicant in response to this Office action.

Claims 1-33 are pending in the instant application and Claims 8-10, 16-33 have been withdrawn from further consideration by the Examiner under 37 CFR 1.142(b) as being drawn to non-elected invention.

Group 26, Claims 1-7, 11-15, are currently under prosecution. Claim 16, drawn to a method detecting prostate cancer, comprising detecting a combination of at least two SMARC markers, has been withdrawn from consideration, as being drawn to non-elected invention.

The traversal is on the following ground(s):

1. Applicant asserts that there are only two SMARC markers, e.g. SMARCD3 or SMARCD1, and therefore, the number of groups of invention would be reduced.
2. Applicant asserts that the Examiner concedes that linking claims are presented that link the SMARC family of markers that exhibit an altered expression associated with prostate cancer. Applicant asserts that thus upon allowance of a linking claim, the

restriction requirements to the linked invention shall be withdrawn with regard to any claims dependent from or otherwise including all the limitation of the allowable linking claims.

3. Applicant asserts that all of the methods that are based on methods for detecting nucleic acids should be grouped together. That is claims 1-7, 11-16 (groups 25-48), claims 17-21 (groups 73-96), claims 22 and 33 (group 98), claim 23 (group 100), and claims 25 and 27 (group 104) should be grouped into one group. Applicant asserts that although there are different objectives, the same methods and reagents are used a) to assess whether a subject is afflicted with prostate cancer, b) to assess the progression of prostate cancer, c) to assess the efficacy of a therapy, d) to assess a potential test compound that may trigger prostate cancer, e) to identify compounds useful for treating prostate cancer. Applicant asserts that the expression levels are all measured, using the same reagents to detect the nucleic acids.

Applicant further asserts that the groups all belong to the same class and subclass, and thus a single search would suffice for all the groups.

Applicant asserts that in addition, claim 24 (group 102) and claims 30-31 (group 106) also involve measuring nucleic acids, and thus should be grouped together with the above groups.

4. Applicant asserts that similar arguments apply for claims 1-10, 16 (groups 1-24), claims 17-21 (groups 49-72), claims 22 and 33 (group 97), claim 23 (group 99), claims 25-26 (group 103), and claims 28-29 (group 105), all in one class 435, subclass 7.1, and should be in one grouped, because even though the method objectives are

different, the reagents and methods used to measure SMARC polypeptide levels remain the same.

Applicant's traverse has been considered, but are found not to be persuasive for the following reasons:

1. Contrary to Applicant arguments, there are five SMARC markers, as disclosed in Ring et al, 1998, IDS# on , which is incorporated by reference to the instant application (specification, p. 7, lines 18-22), i.e. SMARC1, SMARC2, SMARCD1, SMARCD2 AND SMARCD3 (Ring et al, abstract). Further, Applicant discloses that various known SMARC genes are applicable to the instant invention (specification, lines 18-19), and that this invention pertains not only to a SMARC nucleotide sequence alone, but embraces other polynucleotides that have a SMARC nucleotide sequence within them, such as SMARCD3 (specification, lines 24-26). Therefore, based on the disclosure of the instant application, one would reasonably interpret that the claimed SMARC makers encompass all five different SMARC polynucleotides, as taught by Ring et al. Thus the number of groups of invention would be not reduced.
2. The Examiner agrees that claim 1 is a linking claim linking different groups of SMARC markers family, as recited in the Office action of paper No: 10, on 07/29/03, and that if claim 1 is allowable, upon allowance of the linking claim, claim 1, the restriction requirements to the linked invention shall be withdrawn with regard to any claims dependent from or otherwise including all the limitation of the allowable linking claims.

3. Concerning claims 1-7, 11-16 (groups 25-48), claims 17-21 (groups 73-96), claims 22 and 33 (group 98), claim 23 (group 100), and claims 25 and 27 (group 104), claim 24 (group 102) and claims 30-31 (group 106), they are patentably distinct, because not only they have different objectives, their method steps, response variables, criteria for success are not the same. Further, their searches are based on different databases, and not solely on classification search, and are not co-extensive. Therefore it would be a serious burden for the Examiner to search all the groups together.

The requirement is still deemed proper and is therefore made FINAL.

Accordingly, group 26, claims 1-7, 11-15, SMARCD3 are examined in the instant application, wherein claims 1-7, 11-15 are examined only to the extent of a method of detecting prostate cancer, comprising determining the mRNA level of SMARCD3. Claim 16, drawn to a method detecting prostate cancer, comprising detecting a combination of at least two SMARCD markers has been withdrawn from consideration, as being drawn to non-elected invention.

For the purpose of compact prosecution, it is assumed that claim 2 is drawn to a method of claim 1, wherein said marker is a mRNA of SMARCD-3 marker or portion thereof.

## OBJECTION

Claims 1-7, 11-15 are objected to because part of claims 1-7, 11-15 are drawn to non-elected invention, i.e. 1) a method for assessing whether a subject is afflicted with prostate cancer, comprising detecting a difference in protein level of expression of

SMARC markers, 2) a method for assessing whether a subject is afflicted with prostate cancer, comprising detecting a difference in mRNA level of expression of a SMARC that is different from SMARCD-3, e.g. SMARC1, SMARC2, SMARCD1, SMARCD-2, or a combination of different SMARC markers.

### **REJECTION UNDER 35 USC 101, UTILITY**

35 U.S.C. 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title".

Claims 1-7, 11-15 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial asserted utility or a well established utility.

Claims 1-7, 11-15 are drawn to a method for assessing whether a subject is afflicted with prostate cancer, comprising detecting a difference in mRNA level of expression of the transcribed SMARCD-3 marker or a portion thereof, between a normal control sample and a sample from said subject. Said marker corresponds to a transcribed polynucleotide or portion thereof. Said level of expression is assessed by detecting the presence of a transcribed polynucleotide or portion thereof. The transcribed polypeptide is a mRNA or a cDNA. The presence of the transcribed polypeptide or portion thereof is detected by amplification or by detecting the presence

of said transcribed polypeptide, which anneals with said marker or portion thereof, under stringent hybridization conditions. Said sample comprises cells obtained from said subject, or from prostate gland or from blood. Said difference is by a factor of about at least 2 or about at least 3.

The specification discloses cDNA and protein sequence of SMARCD-3, a member of SWI/SNF related matrix associated actin dependent regulator of chromatin family (SMARC). The specification discloses that the SWI/SNF complexes or SMARC interact with chromatin and facilitates the function of transcriptional activators, and are known in the art (p.2, last paragraph, p.7, lines 18-22). The specification discloses that the sequence for SMARCD-3 is available in the public database Genbank with accession number U66619 (p.78, lines 2-4). The specification further discloses that primers specific for SMARCD-3 could be designed based the nucleotide sequence of accession No: U66619 (p.78, last paragraph).

The specification contemplates detection of SMARCD-3 in solid prostate tumor tissues, using the affymetrix microarray in which cRNA are prepared and hybridized to Affymetrix chips (Example 4 on page 79, and page 76, lines 15-26). The specification discloses that SMARCD-3 is down regulated by androgen, using said microarray (p.77, last paragraph).

There is however no data showing actual detection of any differential expression of SMARCD-3 in prostate tumor tissue as compared to normal prostate tissue. It is noted that expression of SMARCD-3 being down-regulated by an androgen is not in any

way correlated with a change in mRNA level of SMARCD-3 in prostate cancer tissue as compared to normal control tissue.

It is well known in the art that not every gene is affected in cancer, including prostate cancer, in view that gene expression is tightly controlled in cells, e.g. at at least four control points, activation of gene structure, initiation of transcription, processing transcript and transport to cytoplasm and translation of mRNA (Lewin, B, ed, 1983, Genes, Wiley & Sons, New York, p. 428-429). In other words, changes in the level of expression of a specific gene associated with cancer is an unpredictable event. Thus one cannot determine that SMARCD3 would have differential expression in prostate cancer as compared to normal tissue, unless tested, i.e. unless further experimentation is done.

In the absence of subjective data to support the claimed detecting a difference in the mRNA level of SMARCD-3 in prostate cancer tissue as compared to normal prostate tissue, one cannot assess the claimed method, and further experimentation is required to demonstrate that there is a difference in the mRNA level of SMARCD-3 in prostate cancer tissue as compared to normal prostate tissue.

Further, the disclosed method using affymetrix microarray in which cRNA are prepared and hybridized to for use to monitor the expression of SMARCD-3 is based on 6000 genes (specification, p.76, lines 25-26), which is under-represented of all mRNAs in a cell. It is known that cells in the human body seem to have approximately 100,000 genes and the differences among different types of cells are believed to reflect the differential expression of the 100,000 or so genes (WO 95/20681, p.2, last paragraph).

Further, a typical conventional cDNA library should have a clone complexity of at least  $10^6$  clones (WO 95/20681, p.4, lines 33-35). Thus it is clear that not all of the 100,000 or so genes is represented. It is noted that from screening underrepresented libraries, a polynucleotide that is not expressed in one library or is expressed in another appears to be an artifact of the analytical system and cannot be extrapolated to a prediction of whether that the polynucleotide is over or underexpressed in the tissue "represented" by the library.

For reasons set forth above the disclosure satisfies none of the criteria for a specific, substantial utility. See *In re Kirk*, 153 USPO 48, 53 (CCPA 1967) (quoting the Board of Patent Appeals, 'We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.'). In *Brenner*, the Court approved a rejection for failure to disclose any utility for a compound where the compound was undergoing screening for possible tumor-inhibiting effects and an adjacent homologue of the compound had proven effective. *Brenner*, 148 USPO at 690. Here, there is no evidence that the claimed method of detecting prostate cancer by detecting a significant difference in the

mRNA level of SMARCD-3 in a sample as compared to a control has any substantial utility.

The specification essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for the disclosed nucleic acids. Because the claimed invention is not supported by a specific, substantial asserted utility for the reasons set forth, credibility of any utility cannot be assessed.

#### **REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, ENABLEMENT**

Claims 1-7, 11-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

**A.** Specifically, since the claimed invention is not supported by a well established utility for the reasons set forth in the rejection under 35 USC 101 above, one skilled in the art clearly would not know how to use the claimed invention for practical benefits.

**B.** Further, one cannot extrapolate the teaching in the specification to the enablement of claims 1-7, 11-15, because **one would not know how to make the invention, due to the lack of disclosure in the claims and in the specification the actual sequence structure of SMARCD-3.**

It is noted that there is no disclosure in the specification what the sequence structure of SMARCD-3 is under sequence listing, nor the structures of primers specific

for SMARCD-3 for use in the claimed method. The specification discloses that SMARCD genes have been elucidated and **incorporates by reference** the publication by Ring et al, 1998, Muchardt et al, 1999, and Wallberg et al, 2000 (p. 7, lines 18-22). The specification further discloses that SMARCD-3 cDNA is available in the sequence database Genbank with accession number U66619, and that the publications and sequence databases provide those of skill in the art with the genes needed (p. 78, first paragraph). Further the specification discloses that primers for SMARCD-3 can be designed based on the sequence of SMARCD-3 available from Genbank Accession number U66619 (p. 73, last two lines under "Quantitative Taqman RT-PCR, p.78, last paragraph).

A review of the references by Ring et al, 1998, Muchardt et al, 1999, and Wallberg et al does not reveal any actual sequence structure of SMARCD-3, except recitation of Genbank Accession number U66619 by Ring et al, p. 140, paragraph before last.

One would not know how to carry out the claimed method, based solely on Genbank sequence number, because a sequence from a particular Genbank sequence accession number could be updated, i.e. changed including deletion of several nucleotides, or the accession number could be removed from Genbank database, due to a request from the inventor of said sequence (see Interview summary with Eric Sayers, a GenBank representative, on 11/24/03). Thus based solely on Genbank sequence accession number, it would not be expected that a polynucleotide sequence based on Genbank accession would remain the same, or available to the public.

Further, the Genbank Accession number U66619 is an essential material for designing primers to use in the claimed method of detection of prostate cancer. However, incorporation by reference of the Genbank Accession number U66619, is improper, according to MPEP 6.19 which teaches that incorporation of **essential material** in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973) (see MPEP 6.19 and 6.19.01).

Given that a sequence of a particular Genbank accession number could change or could be removed from the Genbank database, the lack of adequate disclosure in the specification, and in view of the complex nature of the claimed invention, and little is known in the art about the claimed invention, one of skill in the art would be forced into undue experimentation to practice the claimed invention.

C. Moreover, it is noted that a **difference** in the mRNA level of SMARCD-3 in prostate cancer tissue as compared to normal prostate tissue in claims 1-7, 11-15 encompasses either an increase or a decrease of the mRNA level.

It is further noted that a difference factor of about **at least 2** or of above **at least 3** encompasses a range of any number of factors as long as they are above 2 or 3, for example, 1000 fold difference.

Since one cannot predict whether there is a difference in mRNA level of SMARCD-3 in prostate cancer tissue, as compared to normal prostate tissue, one cannot predict whether said difference is an increase or a decrease in mRNA level of SMARCD-3 in prostate cancer tissue, as compared to normal prostate tissue. Similarly, one cannot predict whether said difference is by a factor of about **at least 2** or above **at least 3**, which reads on a range of any number of factors as long as they are above 2 or 3, for example, 1000 fold difference.

Without further guidance as to whether mRNA level of SMARCD-3 decreases or increases in prostate cancer tissue, as compared to normal prostate tissue, it would not be possible to use the claimed invention.

D. Moreover, claims 1, 3 and dependent claims 2, 6-7, 11-15, as drawn to a method of assessing whether a subject is afflicted with prostate cancer, comprising determining the expression level of SMARCD-3 marker in a sample, or a cell, encompass a method of assessing whether a subject is afflicted with prostate cancer, comprising determining the expression level of SMARCD-3 marker in a sample, wherein said sample comprises **"cells from any tissue" to which prostate cancer has metastasized.**

Since one cannot predict whether there is a difference in mRNA level of SMARCD-3 in prostate cancer tissue, as compared to normal prostate tissue, one cannot predict whether cells from any tissue to which prostate cancer has metastasized,

or metastasized prostate cells would still over- or under-express SMARCD-3, as compared to normal prostate tissue. It is well known in the art that expression of a sequence could be lost during the progression toward metastasis. For example, Kibel, AS et al, 2000, J urol, 164(1): 192-6 teach that gene expression in the chromosomal region 12p12-13 is different in primary and metastatic prostate cancer cells, and that inactivation in the chromosome region 12p12-13 occurs prior to metastasis. Zhai, HE, 1994, J Cell Biochem, Suppl 19: 208-216, teach expression of various biomarkers associated with prostate cancer progression. Zhai et al teach that in prostate cancer, PC-3N35 subclones which are cloned from primary and metastatic sites (lymph node, kidney and bone), show difference in the levels of protein expression of various markers, such as c-erbB, vimentin, ICAM-1, cytokeratin, collagen IV between the parental PC-3N35 clone and its metastatic subclones (p.209 and table 1) and that the subline derived from the metastatic site lymph node has a 12p:17q translocation, whereas the bone-derived subline contains an isochromosome 7q (p.211, first column, first paragraph). Cheung S T et al, 2002, Cancer Research, 62(16): 4711-21, teach that from 63 metastatic clones, 39 known genes and 24 express sequence tags are down-regulated, whereas in other 27 metastatic clones 14 known genes and 13 express sequence tags are up-regulated. Thus one cannot predict whether cells from any tissue to which prostate cancer has metastasized, or metastasized prostate cells would still over- or under-express SMARCD-3, as compared to normal prostate tissue.

It is noted that MPEP 2164.03 teaches that "the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the

state of the art as well as the predictability of the art. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as how to make and use the invention in order to be enabling.

Thus in the absence of objective evidence that there is a difference in mRNA level of SMARCD-3 in prostate cancer tissue as compared to normal prostate tissue, in view of the unpredictability of the existence of said difference, and further in view of the complex nature of the claimed invention, and little is known in the art about the claimed invention, one of skill in the art would be forced into undue experimentation to practice the claimed invention.

E. Moreover, due to the language "a" transcribed polynucleotide in claim 11, claims 11-14 encompass a method of assessing whether a subject is afflicted with prostate cancer, comprising determining the expression level of SMARCD-3 marker, wherein said level of expression is assessed by detecting the presence of "**any unrelated**" transcribed polynucleotide or portion thereof, and wherein a significant difference in the expression level of said marker in a sample and a control sample indicates the presence of prostate cancer.

One cannot extrapolate the teaching in the specification to the scope of the claims 11-14, because the claimed method would detect the expression of unrelated sequences, and thus it is unpredictable that any significant difference in the expression level of said unrelated sequences between prostate cancer and normal control would be detected, because it is well known in the art that not every gene is affected by cancer.

The specification does not disclose a method for assessing whether a subject is afflicted with prostate cancer by detection of any unrelated transcribed polynucleotide other than SMARCD-3 of accession number U66619. The specification does not disclose how to assess whether a subject is afflicted with prostate cancer, wherein the presence of an unrelated transcribed polynucleotide or portion thereof is detected.

Given the unpredictability of the existence of any significant difference in the expression level of unrelated sequences between prostate cancer and normal control, as detected using the claimed method, the lack of adequate disclosure in the specification, and in view of the complex nature of the claimed invention, and little is known in the art about the claimed invention, one of skill in the art would be forced into undue experimentation to practice the claimed invention.

**F. In addition, claim 15 encompasses a method of assessing whether a subject is afflicted with prostate cancer, by detecting unrelated polynucleotide or portion thereof under hybridization conditions that allow annealing of sequences of at least 60%, 70%, 80%, 85% or 90% homology to SMARCD-3 polynucleotide.**

It is noted that the specification discloses that "hybridization under stringent conditions" is intended to describe conditions under which nucleotide sequences at

least 60%, 70%, 80%, 85% or 90% homologous to each other typically remained hybridized to each other (p. 23, lines 16-21).

One cannot extrapolate the teaching in the specification to the scope of the claim 15, because the claimed method would detect the expression of unrelated sequences, or variants of at least 60%, 70%, 80%, 85% or 90% homology to SMARCD-3 marker with unknown structure, and function, that are attached to SMARCD-3 marker, or portion thereof, i.e., sequences hybridized to SMARCD-3 marker, or portion thereof, under stringent hybridization conditions. Thus it is unpredictable that any significant difference in the expression level of said unrelated sequences between prostate cancer and normal control would be detected, because it is well known in the art that not every gene is affected by cancer.

The specification does not disclose how to assess whether a subject is afflicted with prostate cancer, wherein the presence of an unrelated transcribed polynucleotide or portion thereof, i.e. a transcribed polynucleotide that anneals with the claimed marker or portion thereof under stringent hybridization conditions, is detected.

Given the unpredictability of detecting any significant difference in the expression level of unrelated sequences between prostate cancer and normal control, using the claimed method, the lack of adequate disclosure in the specification, and in view of the complex nature of the claimed invention, and little is known in the art about the claimed invention, one of skill in the art would be forced into undue experimentation to practice the claimed invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 703-305-2008. The examiner can normally be reached on 9:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANTHONY CAPUTA can be reached on 703-308-3995. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0916.



MINH TAM DAVIS

PATENT EXAMINER

November 24, 2003

**REMARK**

It is noted the amendment of paper No:11, on 09/17/03 concerning amending SMARC1 to SMARCD1, and SMARC3 to SMARCD3 does not constitute new matter. It is clear that SMARC1 is intended to be SMARCD1, and SMARC3 is intended to be SMARCD3, because they are referred to the same Genbank accession numbers, U66617 and U66619, respectively.

**CONSULTATION WITH SPE ANTHONY CAPUTA AND PRIMARY KAREN CANELLA  
ON 11/21/03**

- 1) The language "normal" in claim 1 would not be objected to or rejected, because it is clear to one of skill in the art what normal prostate cell is.
- 2) The language "correspond" in claim 2 would not be objected to or rejected, because it is clear to one of skill in the art what "correspond" means.

3) Claims 11-14 however would be rejected under written description and scope of enablement for the use of the language "a" transcribed polynucleotide or portion thereof. Futher, since the polynucleotide is rejected, "portion thereof" would be rejected as well. There is no need for a different scope rejection for portion, since it is routine in the art to design proper primers for detection of portion specific for a known full length polynucleotide sequence.

4) Claims 11, 14, 15 would not be rejected for using the language detecting the "presence" a polynucleotide, whereas a difference in the expression level and not the presence is required for the method of claim 1, because it is clear to one of skill in the art what claims 11, 14, 15 mean.

#### **CONSULTATION WITH SPECIALIST BRIAN STANTON ON 11/26/03**

1. The method claims 1-7, 11-15 lacks utility although the product SMARCD-3 has utility (related to apoptosis).
2. Recitation of genbank sequence only, which is an essential material to carry out the claimed method, is an improper incorporation of reference, under 112, first paragraph.
3. Claims 11-14 are rejected under 112, first paragraph for the use of the language detecting "a" transcribed polynucleotide in claim 11, because it reads on detecting unrelated polynucleotide. Written description rejection is not necessary.
4. Claim 13 does not miss a method step. The claim does not have to recite every single step.

5. Claim 15 is rejected under 112, first paragraph, because the claim reads on detecting prostate cancer, by detecting unrelated sequences that are hybridized to the claimed marker. Written description rejection is not necessary.